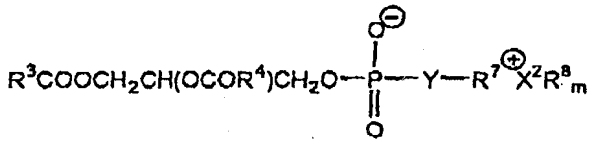
CLAIMS

1. An oral vaccine comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components including cationic compounds and zwitterionic phospholipid in molar ratio in the range 1:1 to 1:5, and comprising

a) at least one cationic compound

b) at least 50% by mole of the zwitterionic phospholipid has the general formula II



II

in which R^3 and R^4 are the same or different and are selected from groups of the formula $CH_3(CH_2)_e(CH_2)_g$-

in which each of e and g are 0 to 23 and e + g is in the range 12 to 23;

R^7 is a C_{1-8} alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-11} aryl or aralkyl, or two or three of the groups R^8 together with X^3 may form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

2. A vaccine according to claim 1 in which the cationic compound has the general formula I,

$$R^1OCH_2CH(OR^2)CH_2R^5X^1R^6{}_n \qquad I$$

in which R^1 and R^2 are the same or different and are selected from groups of the formula $CH_3(CH_2)_a(CH=CH\text{-}CH_2)_b(CH_2)_c(CO)_d$-

in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

R^5 is a bond or a C_{1-8} alkanediyl group;

X^1 is N, P or S;

n is 3 where X^1 is N or P and is 2 where X^1 is S; and

the groups R^6 are the same or different and are selected from hydrogen, C_{1-8} alkyl, C_{6-12} aryl or aralkyl, or two or three of the groups R^6 together with X^1 may form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

3. A vaccine according to claim 2 in which R^1=R^2 and R^3=R^4.

4. A vaccine according to claim 3 in which R^1 and R^2 represent a different group to R^3 and R^4.

5. A vaccine according to claim 3 and claim 4 in which in R^1 and R^2 b=1 and in which (a + c) is in the range 10-20.

6. A vaccine according to any of claims 3 to 5 in which d = 0.

7. A vaccine according to any of claims 2 to 6 in which X^1 is N and in which the R^6 groups are all C_{1-4} alkyl.

8. A vaccine according to any preceding claim which comprises two zwitterionic phospholipids each having the formula II, in which Y is O, and X^2 is N, and the groups R^8 of the first phospholipid are all hydrogen and the groups R^8 of the second phospholipid and all C_{1-4} alkyl, preferably methyl.

9. A vaccine according to claim 8 in which, in each phospholipid Y is O and R^7 is $(CH_2)_h$ in which h is 2 or 3.

10. A vaccine according to claim 8 or claim 9 in which the groups R^3 and R^4 of the first phospholipid are the same and each is a group in which f=1 and (e + g) is in the range 10 to 20, preferably 12 to 14.

11. A vaccine according to any of claims 8 to 10 in which the groups R^3 and R^4 of the second phospholipid are the same and e + g is in the range 15 to 23, preferably 15-17.

12. A vaccine according to any of claims 12 to 14 in which the zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, diplamitoylphosphatidylcholine, dipalmitoylphosphatidylethanolamine and mixtures thereof.

13. A vaccine according to claim 1 in which the cationic compound is cholesterol-3β-N-(dimethyaminoethyl) carbamate.

14. An oral vaccine according to any preceding claim in which the liposome forming components include at least 25 mole%, preferably at least 50 mole%, of components which individually have a transition temperature of more than 40°C.

15. A vaccine according to any preceding claim in which the nucleic acid is entrapped within the liposomes.

16. A method in which a human or a non-human animal is vaccinated by administering a vaccine according to any preceding claim orally whereby an immune response to the encoded antigen is generated.

17. A method of entrapping polynucleotide into liposomes involving the steps of:

i) forming an aqueous suspension comprising naked nucleic acid, which operatively encodes an immunogenic polypeptide useful to induce a desired immune response in a human or animal subject, and preformed liposomes formed of liposome forming components as defined in any of claims 1 to 14,

ii) freeze-drying or spray-drying the suspension, and

iii) rehydrating the product of step ii) to form dehydration/rehydration vesicles.

18. A method according to claim 17 comprising the further steps of:

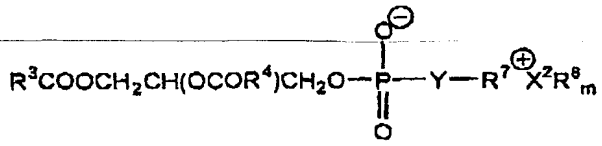
iv) subjecting the aqueous suspension of dehydration/rehydration vesicles from step iii to microfluidization to control their size; and

v) optionally separating non entrapped nucleic acid from liposomes.

19. Use of a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components including cationic compounds and zwitterionic phospholipid in molar ratio in the range 1:1 to 1:5, and comprising

a) at least one cationic compound

b) at least 50% by mole of the zwitterionic phospholipid has the general formula II



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in the manufacture of an oral vaccine for use in the vaccination of an animal in a method in which the vaccine is administered orally.

20. Use according to claim 19 in which the vaccine is as claimed in any of claims 2 to 15.